Guest blogger Jeff Sheehy - CIRM Grantees Show Progress Towards a “Cure for HIV” in Boston

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At the 18th Conference on Retroviruses and Opportunistic Infections (CROI) in Boston, two members of CIRM's HIV/AIDS Disease Team led by John Zaia at City of Hope presented new research showing the team's progress toward the clinic.

The team's overall goal is to use technology developed by Sangamo Biosciences to modify the blood-forming stem cells of people infected with HIV. The modifications would effectively remove the doorway protein-called CCR5-the HIV virus uses to enter immune cells. The less than one percent of the population who lack CCR5 are naturally resistant to HIV infection and one HIV patient in Berlin who received a complete bone marrow transplant from someone born lacking the CCR5 receptor has been functionally "cured" of HIV.

In a presentation on Monday, Sangamo Biosciences released preliminary data from 6 HIV patients in its gene therapy clinical trial targeting T-cells, which are the primary immune cells invaded by the HIV virus. The study uses Sangamo's zinc finger gene modification technique to remove the CCR5 receptor from T-cells taken from the patients with HIV. Those modified T cells were then returned to the patients' blood system. The patients saw both survival and expansion of the modified T-cells-a critical finding since this implies some competitive advantage for cells protected by CCR5 deletion over cells that are not protected.

This finding is not itself a cure, since T-cells are just one type of immune cell that HIV attacks. However, it is encouraging for the CIRM funded Disease Team project, which seeks to use the same gene modification technique on a HIV patient's blood-forming stem cells in the bone marrow. These tissue-specific stem cells give rise to all of the blood cells in the body and modifying them successfully could lead to protection for all of the immune cells that HIV attacks â not just the T cells. A full bone marrow transplant replacing the entire blood-forming stem cell compartment with modified cells carries significant risk, with mortality close to twenty percent. However, partial replacement of the stem cell compartment with CCR5 deleted cells and successful survival and expansion might be a safer and more accessible avenue for replicating the functional cure achieved in the single Berlin patient.

In a presentation Wednesday at CROI supporting this approach, Paula Cannon from USC and a member of the same Disease Team, will expand on her research on the use of hematopoietic stem cells genetically modified with the Sangamo zinc finer technology to remove CCR5 in mice with humanized immune systems. In her previously published study (here's a link to the Nature paper), the partial replacement of the bone marrow stem cell compartment with a minority of gene-modified cells led to competition between modified and unmodified cells with the CCR5 deleted modified cells (here's our blog entry on the work). In the humanized mice, the modified cells were eventually selected to the point where the humanized immune systems of the mice were able to control HIV successfully to a level where HIV is undetectable and without the use of antiretroviral therapies.

Together these two studies suggest that the Sangamo technology is able to effectively remove the CCR5 protein from modified cells, and that those cells are able to resist HIV infection.

Here are a few news reports about the work:
http://www.aidsmeds.com/articles/HIV_Sangamo_CCR5_1667_19952.shtml

http://m.apnews.com/ap/db_8559/contentdetail.htm?contentguid=YVSgAu1f

This video discusses the City of Hope HIV/AIDS disease team:

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Tags: sheehy, university of southern california, HIV/AIDS, sangamo, cannon

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